An *EcoR*I restriction map and sequence-ready substrates of human chromosome 19

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High resolution physical maps of human chromosomes provide the ordered reagents required for detailed analyses of gene organization and furnish the templates for determining the complete DNA sequence. We have developed a cosmid-based ordered physical map that spans approximately 95% of the euchromatin of chromosome 19 (47.5 MB) and that includes complete digest *EcoR*I maps spanning 42 Mb (~83%) of the region. The underlying restriction map defines the minimal number of cosmid clones which are required to sequence the chromosome while minimizing redundant coverage. The present *EcoR*I mapped region is represented by 319 contigs with an average size of 134Kb (range 40-1041 Kb). The clones for selected members of the restriction maps have been anchored to the chromosome by direct FISH or through hybridization to large insert clones that serve as links between the restriction-mapped clones.Thus, the position of each contig is known. Incorporated within the present restriction map are 251 genes, 132 expressed cDNAs, 150 genetic markers and 276 STSs (one STS/180 Kb average).

We will complete the remaining 8 Mb of *EcoR*I restriction coverage of chromosome 19, thereby extending the cosmid coverage of our map, by continuing to convert our available YAC contigs into cosmids. YAC conversion to cosmids is being carried out by interrogating high-density cosmid filter arrays of chromosome 19-specific libraries with Inter-*Alu* PCR and IRS-bubble PCR probes derived from the YACs.

The approach discussed here has enabled the generation of a verified minimum tiling path of cosmids covering greater than 80% of chromosome 19. The present *EcoR*I map includes 76 maps of greater than 150 Kb (average size of 300 Kb).

Current sequencing efforts involve a 1 Mb *EcoR*I mapped region in q13.1 encompassing the CNF gene. Four similarly mapped regions of the chromosome involving the MEF2B gene, OLFR gene family, FHM gene region, and a 2 Mb region including the XRCC1 and ERCC1 DNA repair genes (see poster by Lamerdin et al) are additional foci.

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